JOURNAL OF ENDOVASCULAR THERAPY
A SAGE Publication
An official publication of the ISEVS

Journal of Endovascular Therapy
2020, Vol. 27(2) 287–295

DOI: 10.1177/1526602820902014
www.jevt.org
SAGE

ZILVERPASS Study: ZILVER PTX Stent vs Bypass Surgery in Femoropopliteal Lesions

Marc Bosiers, MD[1], Carlo Setacci, MD[2], Gianmarco De Donato, MD[2], Giovanni Torsello, MD[3], Pierre Galvagni Silveira, MD[4], Koen Deloose, MD[1], Dierk Scheinert, MD[5], Pierfrancesco Veroux, MD[6], Jeroen Hendriks, MD[7], Lieven Maene, MD[8], Koen Keirse, MD[9], Tulio Navarro, MD[10], Joren Callaert, MD[1], Hans-Henning Eckstein, MD[11], Jörg Teβarek, MD[12], Alessia Giaquinta, MD[6], and Jeroen Wauters, MSc[13]

Abstract

Purpose: To report the 12-month results of a multicenter, prospective, randomized controlled trial to determine if the ZILVER PTX paclitaxel-eluting stent was noninferior in terms of safety and efficacy compared with surgical bypass. **Materials and Methods:** This is a study in symptomatic TransAtlantic Inter-Society Consensus (TASC) C and D femoropopliteal lesions comparing endovascular ZILVER PTX stenting vs surgical bypass surgery using a prosthetic graft (*ClinicalTrials.gov* identifier NCT01952457). Between October 2013 and July 2017, 220 patients (mean age 68.6±10.5 years; 159 men) were enrolled and randomized to the ZILVER PTX treatment group (113, 51.4%) or the bypass treatment group (107, 48.6%). Most of the lesions were occlusions (208, 94.5%); the mean lesion length was 247.1±69.3 mm. The primary outcome measure was primary patency at 12 months, defined as no evidence of binary restenosis or occlusion within the target lesion or bypass graft based on a duplex-derived peak systolic velocity ratio <2.4 and no clinically-driven target lesion revascularization (TLR) in endovascular cases or reintervention to restore flow in the bypass. **Results:** The estimated 12-month primary patency rate was 74.5% (95% CI 66.3% to 82.7%) for the ZILVER PTX group vs 72.5% (95% CI 63.7% to 81.3%) for the bypass arm (p=0.998). Freedom from TLR at 12 months was 80.9% (95% CI 73.3% to 88.5%) for the ZILVER PTX group vs 76.2% (95% CI 68.0% to 84.4%) for the bypass group (p=0.471). The 30-day complication rate was significantly lower in the ZILVER PTX group (4.4% vs 11.3%, p=0.004). Also, procedure time and hospital stay were significantly shorter in the ZILVER PTX group (p<0.001 for both). **Conclusion:** With noninferior patency results, a lower complication rate, and shorter procedures and hospital stays, paclitaxel-eluting stenting might become a recommended treatment for long TASC C and D femoropopliteal lesions.

Keywords

bypass surgery, drug-eluting stent, endovascular treatment, femoropopliteal segment, occlusion, peripheral artery disease, stenosis, superficial femoral artery

Introduction

There is a global increase in the prevalence of peripheral artery disease (PAD), with approximately 27 million people in Europe and North America affected.[1] Risk factors contributing to this trend include age, obesity, nicotine abuse, hypertension, hyperlipidemia, diabetes, and family history. Manifestations of PAD range from intermittent claudication to chronic limb-threatening ischemia (CLTI).

The TransAtlantic Inter-Society Consensus II (TASC) recommendations[2] for the treatment of PAD in the femoropopliteal segment are well established in the vascular community. Endovascular therapy is preferred for TASC A and B lesions, but for more challenging TASC C and D lesions surgical treatment is recommended. However, these guidelines from 2007 were based on old endovascular techniques. Today, with the introduction of newer devices and drug-eluting technologies, some endovascular treatments have demonstrated their safety and effectiveness in single-arm and randomized studies vs balloon angioplasty in the femoropopliteal segment.

Early studies with the drug-eluting ZILVER PTX stent (Cook Medical, Bloomington, IN, USA) in femoropopliteal TASC C and D lesions yielded good results, with a 12-month

Correction (February 2025): Article updated online to correct the affiliation of the author "Alessia Giaquinta" from "UFSC University Hospital Santa Catarina, Florianópolis, SC, Brazil" to "University Hospital of Catania, Italy".

primary patency rate of 77.6% in complex lesions with a mean length of 226.1 mm.[3] In another study,[4] 1075 lesions with a mean length of 147 mm were treated with the ZILVER PTX stent, achieving a 12-month primary patency rate of 86.4%. Based on these results, a randomized controlled trial was established to determine if the ZILVER PTX paclitaxel-eluting stent was noninferior to surgical bypass.

Materials and Methods

Study Design

ZILVERPASS was a global, prospective, randomized, controlled, noninferiority study involving patients enrolled at 13 clinical sites in Belgium (n=5), Germany (n=4), Italy (n=2), and Brazil (n=2). The study was conducted in accordance with the Declaration of Helsinki. The local ethical committees at the participating sites approved the study protocol, and all patients provided written informed consent to undergo any study-related procedures. The trial was registered on the National Institutes of Health website (*ClinicalTrials.gov* identifier NCT01952457).

To achieve a homogeneous control group, one type of bypass graft was selected based on the literature comparing polytetrafluoroethylene (PTFE) with Dacron for above-the-knee femoropopliteal bypass.[5–7] Since the primary and secondary patency rates were not significantly different, the study designers opted for prosthetic bypass grafts as the comparator vs the ZILVER PTX stent.

Candidates for the study underwent a baseline clinical examination including medical and medication histories, physical examination, clinical categorization of limb ischemia (Rutherford category), resting ankle-brachial index (ABI), and preoperative duplex ultrasound. Patients were eligible for the study when (1) no underlying medical condition was present that would prevent performing the required testing or completing the study, (2) all general and angiographic inclusion criteria were met, and (3) none of the exclusion criteria was fulfilled. Table 1 gives an overview of the inclusion and exclusion criteria. In brief, patients with moderate to severe intermittent claudication or CLTI with rest pain or minor tissue loss (Rutherford categories 2 to 5) presenting with a long (≥15 cm) stenotic or occlusive de novo lesion (TASC C and D) in the femoropopliteal arteries suitable for both endovascular therapy and bypass surgery could be included in this study.

To determine if the effect of treatment with the ZILVER PTX paclitaxel-eluting stent was not inferior to the effect of treatment with surgical bypass, a sample size of 220 patients was calculated, assuming that the primary patency rates for the bypass arm and the ZILVER PTX arm were 70.0% and 80.0%, respectively. The null hypothesis was that the primary patency rate for the ZILVER PTX arm was 6.0% lower than the primary patency rate for the bypass arm; the study had a power of 86.5% to reject the null hypothesis.

Study Devices

The ZILVER PTX stent is a self-expanding nitinol stent coated with polymer-free paclitaxel (3 μg/mm^2 dose density) and designed to provide support while maintaining flexibility in the vessel on deployment. After deployment, the stent imparts an outward radial force on the inner lumen of the vessel, establishing patency in the stented region. The device is approved by the Conformité Européenne for use in patients with atherosclerotic disease of the above-the-knee femoropopliteal arteries.

The device used for the control arm was a prosthetic bypass from the common femoral artery to the above-the-knee popliteal artery (P1 segment). The type of prosthetic bypass (Dacron or expanded polytetrafluoroethylene) was at the physician's discretion.

Randomization and Masking

Using a computer-generated list for each site, permuted block randomization was applied with block sizes of 8

[1]A.Z. Sint-Blasius Hospital, Dendermonde, Belgium
[2]University of Siena, Italy
[3]St. Franziskus Hospital Münster, Germany
[4]UFSC University Hospital Santa Catarina, Florianópolis, SC, Brazil
[5]University Hospital of Leipzig, Germany
[6]University Hospital of Catania, Italy
[7]University Hospital of Antwerp, Edegem, Belgium
[8]OLV Hospital Aalst, Belgium
[9]RZ Heilig Hart Tienen, Belgium
[10]Federal University of Minas Gerais, Brazil
[11]Klinikum rechts der Isar, Munich, Germany
[12]St. Bonifatius Hospital Lingen, Lingen, Niedersachsen, Germany
[13]Flanders Medical Research Program, Dendermonde, Belgium

Corresponding Author:
Marc Bosiers, A.Z. Sint-Blasius Hospital, Kroonveldlaan 50, Dendermonde 9200, Belgium.
Email: marc.bosiers@telenet.be

Table 1. Inclusion and Exclusion Criteria.

Inclusion criteria: General	
1	Patient presenting with lifestyle-limiting claudication, rest pain or minor tissue loss (Rutherford category 2 to 5)
2	Patient is willing to comply with specified follow-up evaluations at the specified times
3	Patient is >18 years old
4	Patient understands the nature of the procedure and provides written informed consent prior to enrollment in the study
5	Patient has a projected life expectancy of at least 24 months
6	Noninvasive lower extremity arterial studies (resting or exercise) demonstrate ankle-brachial index ≤0.8
7	Patient is eligible for treatment with the ZILVER PTX paclitaxel-eluting stent (Cook) or with surgical above-the-knee bypass placement
8	Male, infertile female, or female of childbearing potential practicing an acceptable method of birth control with a negative pregnancy test within 7 days prior to study procedure
Inclusion criteria: Angiographic	
1	Stenotic or occlusive de novo lesion located in the femoropopliteal arteries, suitable for endovascular therapy and for bypass surgery
2	Total target lesion length is at least 15 cm
3	Minimum of 1.0 cm of healthy vessel (non-stenotic) both proximal and distal to the treatment area
4	P2 and P3 are patent and there is angiographic evidence of at least 1 vessel runoff to the foot that does not require intervention (<50% stenotic)
5	Target vessel diameter visually estimated to be >4 mm and <9 mm at the proximal and distal treatment segments within the SFA
Exclusion criteria	
1	Untreated flow-limiting aortoiliac stenotic disease
2	Any previous surgery and endovascular procedure in the target vessel
3	Severe ipsilateral common/deep femoral disease requiring surgical reintervention
4	Perioperative unsuccessful ipsilateral percutaneous vascular procedure to treat inflow disease just prior to enrollment
5	Femoral or popliteal aneurysm located at the target vessel
6	Nonatherosclerotic disease resulting in occlusion (eg, embolism, Buerger's disease, vasculitis)
7	No patent tibial arteries (>50% stenosis)
8	Prior ipsilateral femoral artery bypass
9	Severe medical comorbidities (untreated CAD/CHF, severe COPD, metastatic malignancy, dementia, etc) or other medical condition that would preclude compliance with the study protocol or 2-year life expectancy
10	Serum creatinine >2.5 mg/dL within 45 days prior to study procedure unless the subject is currently on dialysis
11	Major amputation (above the transmetatarsal) in the study or nonstudy limb
12	Any previously known coagulation disorder, including hypercoagulability
13	Contraindication to anticoagulation or antiplatelet therapy
14	Known allergies to stent components (nickel-titanium, paclitaxel, etc) or bypass graft components (Dacron, ePTFE, etc)
15	Known allergy to contrast media that cannot be adequately premedicated prior to the study procedure
16	Currently participating in another clinical research trial
17	Angiographic evidence of intra-arterial thrombus or atheroembolism from inflow treatment
18	Any planned surgical intervention/procedure within 30 days of the study procedure
19	Target lesion access in the ZILVER PTX stent arm not performed by transfemoral approach

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; ePTFE, expanded polytetrafluoroethylene; SFA, superficial femoral artery.

patients assigned in a 1:1 fashion to either endovascular treatment with the ZILVER PTX stent or bypass surgery with a synthetic graft. Each site received closed envelopes that were opened only after the patient signed the informed consent. Once a treatment was assigned, crossover was not permitted. Patients assigned to the ZILVER PTX group were considered enrolled when successful lesion passage was achieved, and diagnostic angiography confirmed that all angiographic inclusion criteria were met.

Procedures

Standard procedures were followed based on the instructions for use for the devices. Intraoperative heparinization (5000 units) was applied in both treatment groups. The only pretreatment allowed prior to placement of the ZILVER PTX stent was standard balloon angioplasty; no reentry or atherectomy devices were permitted. The use of pre- and postdilation was recommended but at the physician's discretion.

Angiography immediately after the endovascular intervention was required to evaluate the postoperative lesion. Following treatment, antiplatelet therapy consisting of clopidogrel for at least 60 days and lifelong aspirin was routinely prescribed. Physical examination was performed prior to discharge. The follow-up data collection points were 1, 6, 12, 24, 36, and 60 months, with unplanned or interim visits as needed for recurrent symptoms or complications. Follow-up visits included ABI measurements, Rutherford category assessment, and duplex ultrasound examination.

Outcome Definitions

The primary outcome measure of the study was primary patency at 12 months. For the ZILVER PTX arm, this was defined as no evidence of binary restenosis or occlusion within the target lesion based on a duplex-derived peak systolic velocity ratio (PSVR) <2.4 and no clinically-driven target lesion revascularization (TLR). In the bypass arm, patency was no evidence of binary restenosis or occlusion at the anastomoses or over the entire length of the bypass graft based on a PSVR <2.4 and no clinically-driven reintervention to restore flow in the bypass.

Secondary outcomes were (1) device malfunction or serious device-related or other adverse events within 30 days postprocedure; (2) technical success (stent arm: residual stenosis ≤30% by angiography or <50% by ultrasound; bypass arm: no graft lesion and a low resistance blood flow pattern in the distal graft and outflow artery, a residual stenosis <50% evidenced on duplex); (3) 30-day complications (eg, infection or hematoma requiring intervention); (4) primary assisted and secondary patency rates at 1, 6, 12, and 24 months; (5) TLR rate at 1, 6, 12, and 24 months; and (6) clinical success at follow-up, defined as an improvement in the Rutherford category at 1, 6, 12, and 24 months.

Patient Enrollment

Between October 2013 and July 2017, 220 patients (mean age 68.6±10.5 years; 159 men) were enrolled and randomized to the ZILVER PTX treatment group (113, 51.4%) or the bypass treatment group (107, 48.6%). A flowchart of patient enrollment is presented in Figure 1, and patient characteristics are presented in Table 2. The most prominent risk factor was nicotine abuse (164, 74.5%), followed by hypertension (161, 73.2%) and hypercholesterolemia (127, 57.7%). The majority of the patients were claudicants (139, 63.2%), but the bypass patients had significantly more CLTI, as well as hypertension, hypercholesterolemia, and obesity. Most of the lesions (Table 3) were occlusions (208, 94.5%). Overall mean lesion length was 247.1±69.3 mm and did not differ between the groups.

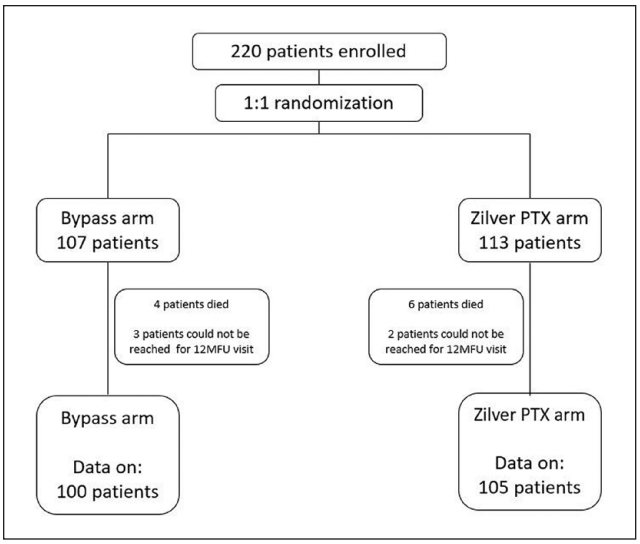


Figure 1. Study flowchart. MFU, months of follow-up.

Statistical Analysis

Continuous data are presented as the mean ± standard deviation (range); categorical data are given as the number (percentage). The primary patency rates were estimated using Kaplan-Meier survival analysis; the estimates are given with the 95% confidence interval. Curves were compared using the log-rank test. Subanalyses were performed to evaluate differences in primary patency based on baseline characteristics (smoking history, hypertension, diabetes, renal insufficiency, obesity, hypercholesterolemia), symptom status (claudication vs CLTI), and presence of total occlusions. The threshold of statistical significance was $p<0.05$. All statistical analyses were completed with IBM SPSS Statistical Software for Windows (version 22.0; IBM Corporation, Armonk, NY, USA).

Results

The technical success rate was 100% in both arms, meaning all occlusions were crossed in the endovascular group. In the 113-patient stent arm, vessel preparation was performed in 105 (92.9%) and postdilation in 104 (92.0%). Procedure time (Table 3) was significantly shorter in the ZILVER PTX group (59.6 vs 123.0 minutes, $p<0.001$), as was the mean hospital stay (2.5 vs 8.1, $p<0.001$).

The 30-day complication rate was significantly higher in the bypass group (11.3% vs 4.4%, p=0.004; Figure 2). In the ZILVER PTX patients, complications consisted of 2 puncture site complications, 2 perforations/dissections after postdilation, and 1 stent thrombosis. Complications in the bypass group were mainly infections (n=5), lymphedema (n=2), graft thrombosis (n=2), stenosis (n=1) or occlusion (n=1), and hematoma (n=1).

Table 2. Baseline Patient Characteristics.[a]

	Total (n=220)	ZILVER PTX (n=113)	Bypass (n=107)	p
Age, y	68.6±10.5	69.6±10.8	67.6±10.1	0.305
Men	159 (72.3)	78 (69.0)	81 (75.7)	0.267
Claudication	139 (63.2)	80 (70.8)	59 (55.1)	0.016
CLTI	81 (36.8)	33 (29.2)	48 (44.9)	
Smoking history	164 (74.5)	78 (69.0)	86 (80.4)	0.053
Hypertension	161 (73.2)	74 (65.5)	87 (81.3)	0.008
Diabetes	65 (29.5)	31 (27.4)	34 (31.8)	0.480
Coronary artery disease	58 (26.4)	26 (23.0)	32 (29.9)	0.246
Cerebrovascular disease	14 (6.4)	8 (7.1)	6 (5.6)	0.655
Renal insufficiency	24 (10.9)	11 (9.7)	13 (12.1)	0.566
Obesity	30 (13.6)	10 (8.8)	20 (18.7)	0.033
Hypercholesterolemia	127 (57.7)	57 (50.4)	70 (65.4)	0.025

Abbreviation: CLTI, chronic limb-threatening ischemia.
[a]Continuous data are presented as the mean ± standard deviation; categorical data are given as the number (percentage).

Table 3. Lesion and Procedure Characteristics.[a]

	Total (n=220)	ZILVER PTX (n=113)	Bypass (n=107)	p
Study limb				
Left	114 (51.8)	61 (54.0)	53 (49.5)	0.509
Right	106 (48.2)	52 (46.0)	54 (50.6)	
Lesion type				
Stenosis	12 (5.5)	9 (8.0)	3 (2.8)	0.092
Occlusion	208 (94.5)	104 (92.0)	104 (97.2)	
TASC C	12	9	3	
TASC D	208	104	104	
Lesion length, mm	247.1±69.3 (100–500)	241.7±63.3 (120–500)	252.9±74.9 (100–400)	0.104
Proximal RVD, mm	5.9±0.7 (4.0–8.0)	5.7±0.7 (4.4–8.0)	6.1±0.8 (4.0–8.0)	0.320
Procedure time, min	90.5±44.8 (17–240)	59.6±22.7 (17–135)	123.1±38.9 (53–240)	<0.001
Hospital stay, d	5.3±5.7 (0–34)	2.5±3.5 (0–20)	8.1±6.0 (1–34)	<0.001
Bypass material (Dacron/PTFE)	NA	NA	42/65	

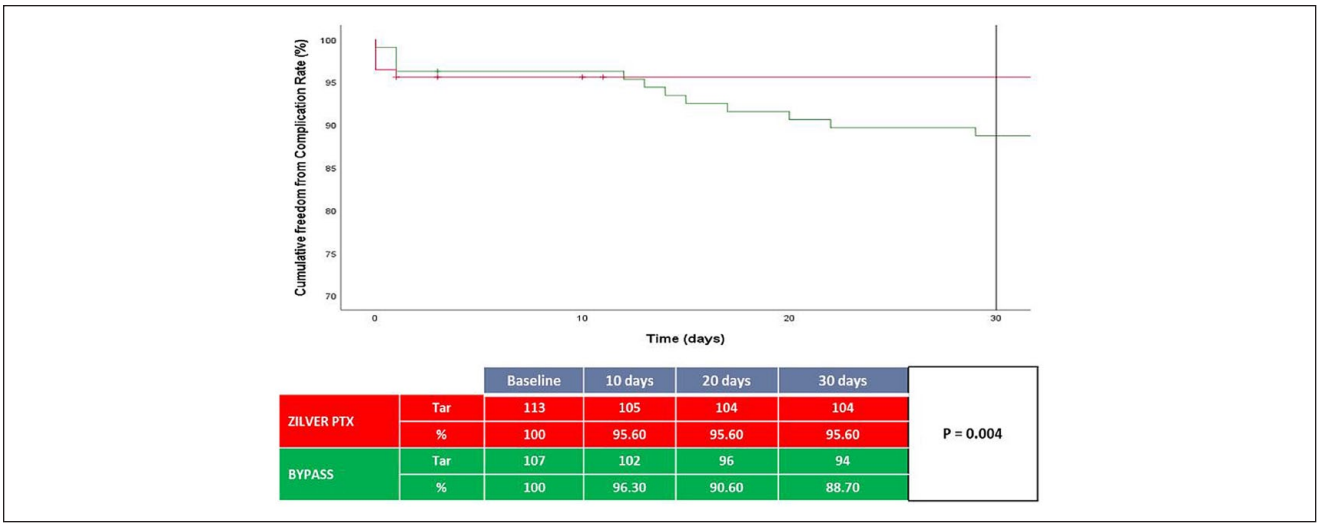
Abbreviations: NA, not applicable; PTFE, polytetrafluoroethylene; RVD, reference vessel diameter; TASC, TransAtlantic Inter-Society Consensus.
[a]Continuous data are presented as the mean ± standard deviation (range); categorical data are given as the number (percentage).

The estimated 12-month primary patency rate (Figure 3) was 74.5% (95% CI 66.3% to 82.7%) for the ZILVER PTX group vs 72.5% (95% CI 63.7% to 81.3%) for the bypass arm (p=0.998). Secondary patency estimates at 12 months were 95.1% (95% CI 91.0% to 99.3%) for the ZILVER PTX group vs 95.9% (95% CI 91.9% to 99.8%) for the bypass group (p=0.754). There were no stent fractures seen in the ZILVER PTX group at 12 months. Subanalysis of primary patency outcomes according to baseline variables did not find any notable differences between the treatment groups.

Freedom from TLR at 12 months was 80.9% (95% CI 73.3% to 88.5%) for the ZILVER PTX group vs 76.2% (95% CI 68.0% to 84.4%) for the bypass group (p=0.471). Freedom from major amputation at 12-month follow-up did not differ between groups [98.1% (95% CI 95.4% to 100%) vs 98.0% (95% CI 95.3% to 100%) for the ZILVER PTX and the bypass groups, respectively; p=0.667]. In total, 4 major amputations were performed within the first 12 months, equally divided in the treatment groups. ZILVER PTX patients undergoing amputation were classified as Rutherford categories 4 and 5, respectively, at baseline; the same was true in the bypass arm.

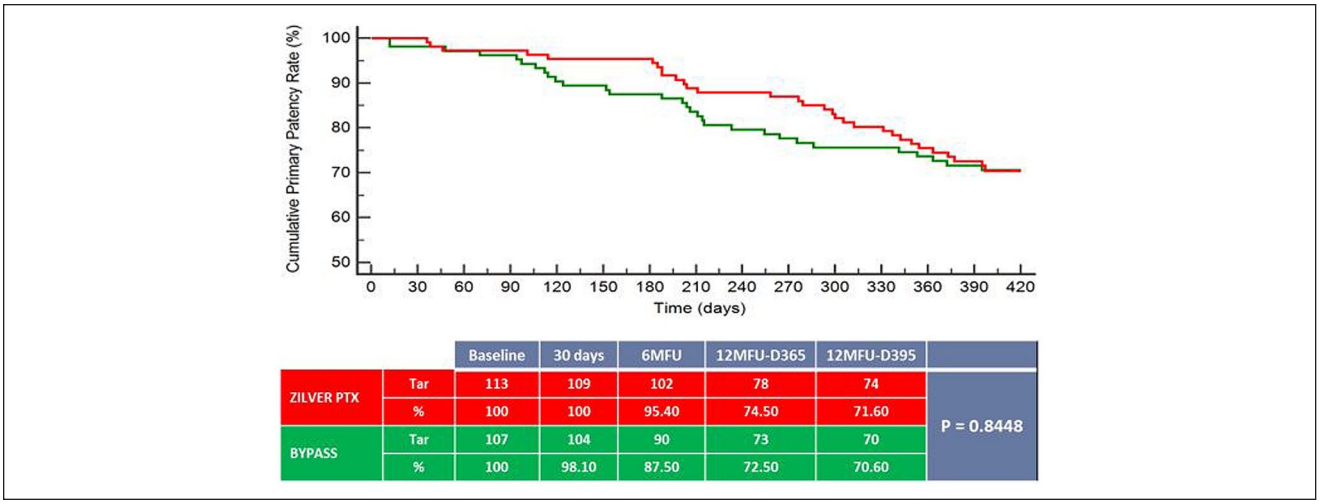
There was no significant difference (p=0.378) in survival rate at 12 months between the ZILVER PTX group (94.5%, 95% CI 90.2% to 98.8%) and the bypass group (96.1%, 95% CI 92.3% to 99.9%). None of the deaths was categorized as related to the procedure or device.

Among the clinical outcomes at 12-month follow-up, paired ABI measurements were available in 164 of 220 patients; of these, 150 (91.1%) had an increased ABI at 12 months (mean 0.354). Only 14 patients had a decrease in



		Baseline	10 days	20 days	30 days	
ZILVER PTX	Tar	113	105	104	104	P = 0.004
	%	100	95.60	95.60	95.60	
BYPASS	Tar	107	102	96	94	
	%	100	96.30	90.60	88.70	

Figure 2. Thirty-day complication rate. Tar, total at risk.



		Baseline	30 days	6MFU	12MFU-D365	12MFU-D395	
ZILVER PTX	Tar	113	109	102	78	74	P = 0.8448
	%	100	100	95.40	74.50	71.60	
BYPASS	Tar	107	104	90	73	70	
	%	100	98.10	87.50	72.50	70.60	

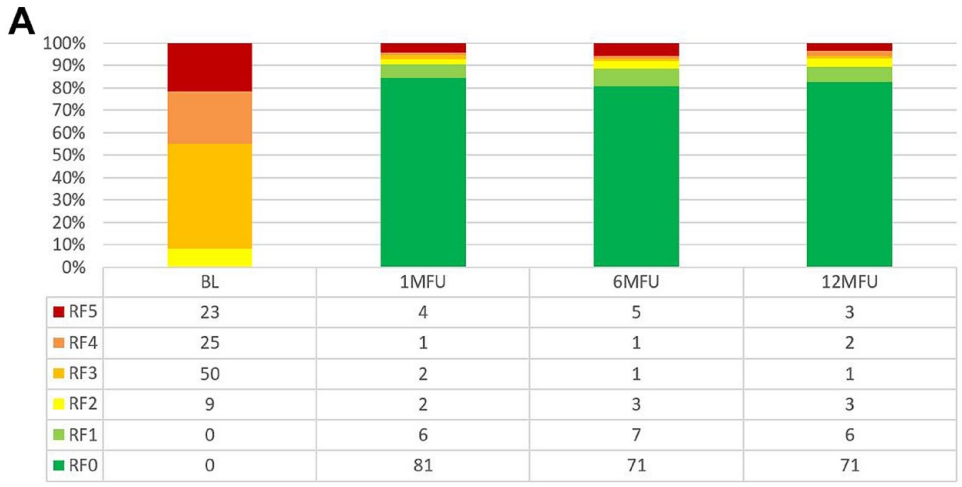
Figure 3. Twelve-month primary patency rate. D, days; MFU, months of follow-up. Tar, total at risk.

ABI. In both treatment groups the same improvement in ABI was seen: 85.0% (mean 0.343) in the ZILVER PTX group and 96.1% (mean 0.368) the bypass group.

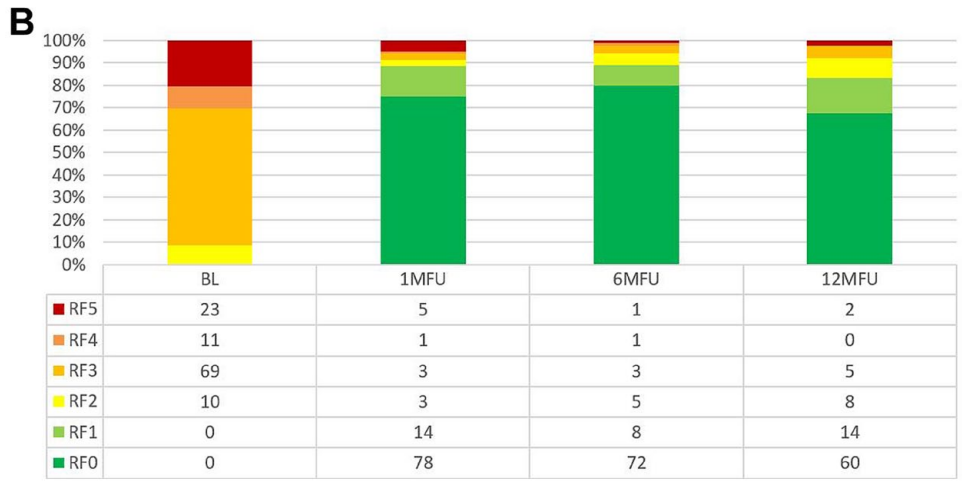
In terms of Rutherford classification, a positive evolution was seen within the first 12 months, with 132 (92.6%) of 172 patients improved by at least 1 Rutherford category. These results were mirrored in the treatment groups, with 91.9% of the bypass patients (Figure 4A) and 93.3% of the ZILVER PTX patients (Figure 4B) demonstrating a ≥1 category improvement.

Discussion

Surgical treatment with prosthetic bypass grafts has yielded good results in numerous trials. Berglund et at[6] retrospectively analyzed 499 patients who received an above-knee femoropopliteal bypass with a saphenous vein graft (139 subjects) or an expanded PTFE (ePTFE) graft (360 subjects). Primary patency estimates after 12 months were 87% and 75% for the venous and prosthetic grafts, respectively. Jensen et al[7] investigated 427 patients in a randomized trial with patients who underwent an above-knee femoropopliteal bypass (205 PTFE and 208 Dacron; 14 patients were excluded). The primary patency rates after 12 months were 70% and 78% for PTFE and Dacron, respectively. Kedora et al[8] compared 86 patients (100 limbs) with femoropopliteal occlusive disease in a randomized trial. Fifty limbs were treated with angioplasty and one or more self-expanding stent-grafts, the other 50 limbs were treated with a synthetic Dacron or ePTFE bypass graft. After 12 months, the primary patency for the bypass group was 74.2%. In a similar study design, McQuade et al[9] randomized 100 limbs (86



	BL	1MFU	6MFU	12MFU
RF5	23	4	5	3
RF4	25	1	1	2
RF3	50	2	1	1
RF2	9	2	3	3
RF1	0	6	7	6
RF0	0	81	71	71



	BL	1MFU	6MFU	12MFU
RF5	23	5	1	2
RF4	11	1	1	0
RF3	69	3	3	5
RF2	10	3	5	8
RF1	0	14	8	14
RF0	0	78	72	60

Figure 4. Rutherford (RF) category evolution in the (A) bypass group vs the (B) ZILVER PTX group. BL, baseline; MFU, months of follow-up.

patients) with superficial femoral artery (SFA) occlusive disease to treatment with stent-grafts or a synthetic Dacron or ePTFE bypass graft. The bypass arm had 12-month primary patency of 77%. A total of 27 patients with TASC D lesions in the SFA were analyzed by Hines et al.[10] All patients received a bypass with an endoscopic saphenous vein. After 12 months the primary patency was 73.2%. In a study by Midy et al,[11] the authors compared the efficacy of prosthetic and autologous vein for above-the-knee femoropopliteal bypasses. With 5-year secondary patency rates of 84.6% and 70.8% for the prosthetic group and autologous vein group, respectively, they concluded that there was no significant difference between the treatment modalities.

Importantly, there is a difference in the patency definition when comparing surgical and endovascular study results. Surgical primary patency is measured by assessing the presence of flow through the bypass. Endovascular primary patency is measured by the absence of binary restenosis (PSVR $\geq$2.4). Bosiers et al[12] examined 100 "patent" surgical bypasses and determined that 89% of them were also patent by the endovascular measure (PSVR $<$2.4), but 11% were stenosed according to the PSVR. This analysis showed a ~10% margin of error that can be taken into account when interpreting the primary patency of surgical bypasses.

Dake et al[13] examined 900 lesions (mean lesion length 99.5$\pm$82.1 mm) in the femoropopliteal segment treated with one or more ZILVER PTX stents. The primary patency after 12 months was 86.2%. Also, the ZILVER PTX single-arm study[3] in long and complex femoropopliteal TASC C and D lesions (mean length 226.1$\pm$43.6 mm) recorded good results, with a 12-month primary patency rate of 77.6%. Similarly, Yokoi et al[4] implanted the ZILVER PTX stent in 1075 lesions with a mean length of 147$\pm$97 mm; 12-month primary patency was 86.4%. In that study, 42% of the lesions were longer than 150 mm and 30% were longer than 200 mm.

The ZILVERPASS study confirmed that ZILVER PTX stent results are at least noninferior to bypass results in terms of primary patency and freedom from TLR. When focusing on safety, there were significantly more complications in the first 30 days after surgical bypass than after endovascular treatment. Also, hospital stay and procedure time were significantly shorter in the endovascular treatment group.

These promising results for endovascular treatment were also demonstrated in the SuperB randomized controlled trial[14] comparing the Viabahn endograft with bypass surgery in long and complex femoropopliteal lesions in 126 patients. The noninferiority of Viabahn was reflected in the 12-month primary patency rates of 84.6% for the surgical bypass group and 82.5% for the endovascular group (p=0.978) and freedom from TLR of 67.7% for the surgical group and 75.7% for the endovascular group (p=0.455). Future studies should compare different endovascular treatment modalities for TASC C and D femoropopliteal lesions.

Although bypass treatment has been considered the gold standard for treating long and complex TASC C and D femoropopliteal lesions, recent paclitaxel-eluting stents challenge this position. With lower complication rates in the first 30 days and comparable patency and freedom from TLR results at 12 months, endovascular treatment with ZILVER PTX stenting has a confirmed role in this therapeutic area. Also, shorter procedures and hospital stays both have a substantial impact on patient comfort and a financial impact for health economics models, which should be integrated in the decision-making of the investigator.

A recent publication by Katsanos et al[15] concluded that there is an increased risk of death following the application of paclitaxel-coated devices in the femoropopliteal segment. Our findings in terms of survival, though in a limited follow-up period, do not support this statement. Longer follow-up is necessary.

Limitations

A limitation of this study is that the patient populations differed between the treatment arms. More patients treated with surgical bypass were hypertensive, hypercholesterolemic, obese, and suffering from CLTI compared to the ZILVER PTX stenting group. However, stratification of claudicants vs CLTI patients found no difference between bypass surgery and ZILVER PTX stenting in terms of primary patency.

Another limitation of this study was the use of prosthetic bypass grafts for the control arm. Although venous bypass is still recommended for above-the-knee bypass, a prosthetic bypass was chosen in this study for 2 reasons. Firstly, in the participating centers, it was common to use prosthetic bypass for above-the-knee bypass so as to save a saphenous vein for future below-the-knee bypass. Secondly, as mentioned above, some studies have demonstrated that there is no difference between prosthetic and venous conduits in terms of patency.

Conclusion

If longer-term follow-up confirms that there is no safety concern for these paclitaxel devices, the excellent results of the ZILVER PTX stent confirmed in this study will challenge bypass surgery in long and complex femoropopliteal lesions.

Authors' Note

This study was presented at several meetings. A complete listing is presented in Supplementary Table 1 (available in the online version of the article).

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Pierre Galvagni Silveira received research, clinical trial, or drug study funds from Cook Medical. Giovanni Torsello received research grants from Cook Medical. Dr Koen Deloose is a clinical trial investigator, consultant, and lecturer for Cook Medical. Dierk Scheinert is a consultant for Cook Medical. Tulio Navarro received research grants from Cook Medical.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Marc Bosiers https://orcid.org/0000-0002-4554-6467
Giovanni Torsello https://orcid.org/0000-0001-7513-5063
Koen Deloose https://orcid.org/0000-0001-5434-7323
Jeroen Hendriks https://orcid.org/0000-0001-9145-3643

Supplemental Material

The online materials are available at http://journals.sagepub.com/doi/suppl/10.1177/1526602820902014

References

1. Belch JJF, Topol EJ, Agnelli G, et al. Critical issues in peripheral arterial disease detection and management: a call to action. *Arch Intern Med*. 2003;163:884–892.
2. Norgren L, Hiatt WR, Dormandy JA, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg*. 2007;45(suppl S):S5–S67.
3. Bosiers M, Peeters P, Tessarek J, et al; Zilver PTX Single-Arm Study Investigators. The Zilver PTX Single Arm Study: 12-month results from the TASC C/D lesion subgroup. *J Cardiovasc Surg (Torino)*. 2013;54:115–122.
4. Yokoi H, Ohki T, Kichikawa K, et al. Zilver PTX post-market surveillance study of paclitaxel-eluting stents for treating femoropopliteal artery disease in Japan: 12-month results. *JACC Cardiovasc Interv*. 2016;9:271–277.

5. Green RM, Abbott WM, Matsumoto T, et al. Prosthetic above-knee femoropopliteal bypass grafting: five-year results of a randomized trial. *J Vasc Surg*. 2000;31:417–425.
6. Berglund J, Björck M, Elfström J. Long-term results of above knee femoropopliteal bypass depend on indication for surgery and graft-material. *Eur J Vasc Endovasc Surg*. 2005;29: 412–418.
7. Jensen LP, Lepäntalo M, Fossdal JE, et al. Dacron or PTFE for above-knee femoropopliteal bypass. A multicenter randomised study. *Eur J Vasc Endovasc Surg*. 2007;34:44–49.
8. Kedora J, Hohmann S, Garrett W, et al. Randomized comparison of percutaneous Viabahn stent grafts vs prosthetic femoral-popliteal bypass in the treatment of superficial femoral arterial occlusive disease. *J Vasc Surg*. 2007;45:10–16.
9. McQuade K, Gable D, Hohman S, et al. Randomized comparison of ePTFE/nitinol self-expanding stent graft vs prosthetic femoral-popliteal bypass in the treatment of superficial femoral artery occlusive disease. *J Vasc Surg*. 2009;49: 109–115.
10. Hines GL, Wain RA, Montecalvo J, et al. Femoral-popliteal bypass with endoscopically harvested saphenous vein in patients with TASC D disease of the superficial femoral artery. *Ann Vasc Surg*. 2010;24(5):615–620.
11. Midy D, Papon X, Patra P, et al; Association Universitaire de Recherche en Chirurgie Vasculaire (AURC). Randomized study of noninferiority comparing prosthetic and autologous vein above-knee femoropopliteal bypasses. *Ann Vasc Surg*. 2016;31:99–104.
12. Bosiers M, Deloose K, Callaert J, et al. How to compare results from open with endovascular procedures? [published online May 9, 2019]. *J Cardiovasc Surg (Torino)*. doi:10.23736/S0021-9509.18.10525-8.
13. Dake MD, Scheinert D, Tepe G, et al; Zilver PTX Single-Arm Study Investigators. Nitinol stents with polymer-free paclitaxel coating for lesions in the superficial femoral and popliteal arteries above the knee: twelve-month safety and effectiveness results from the Zilver PTX single-arm clinical study. *J Endovasc Ther*. 2011;18:613–623.
14. Reijnen M. Comparing endoluminal to open fempop bypasses: final 2-year results of the SUPER B trial. Paper presented at: LINC 2018; January 2, 2018; Leipzig, Germany.
15. Katsanos K, Spiliopoulos S, Kitrou P, et al. Risk of death following application of paclitaxel-coated balloons and stents in the femoropopliteal artery of the leg: a systematic review and meta-analysis of randomized controlled trials. *J Am Heart Assoc*. 2018;7:e011245. doi:10.1161/JAHA.118.011245.